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Increased incidence of cervical cytological abnormalities in women with genital warts

I was interested to read the study by Rowen *et al*¹ showing a higher rate of smear abnormalities in women with or contacts of genital warts. Their observations agree with my own (Griffiths M, MD thesis, University of London), where I found abnormal smears in 28% of women with warts and only 9% of controls. Both studies effectively repeat the findings of Franceschi and colleagues² who found an excess of abnormal smears (largely of “superficial dyskaryosis”) in women with warts compared with other STD clinic attenders, though a review of their paper demonstrates that high grade abnormalities were more common in controls.

However, we have shown no difference in the risk of cervical epithelial disease between the two groups,³ when judged by colposcopy and histology. We hypothesised that the reason for this apparent discrepancy might, at least in part, be due to more cautious examination and reporting of smears coming from women known to have warts, resulting in a relative over-reporting of (particularly minor) abnormalities by cytologists. This hypothesis was supported by the findings of a pilot study in which smears from women with warts were sent to cytology with clinical details of either “warts” or “routine” according to prior randomisation. The study showed an excess of “abnormal” smears among “warts” patients but this difference just failed to reach statistical significance owing to sample size.

I believe that cytologists are more likely to report abnormal smears if the clinical information given refers to a history of warts, and therefore would be interested to know whether the cytologist in this particular study was blind to clinical information concerning the patients’ history of warts.

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- 1 Rowen D, Carne CA, Sonnex C, Cooper P. Increased incidence of cervical cytological abnormalities in women with genital warts or contact with warts: a need for increased vigilance? *Genitourin Med* 1991;67:460–3.
- 2 Franceschi S, Doll R, la Vecchia C. *et al*. Genital warts and cervical neoplasia: an epidemiological study. *Br J Cancer* 1983;48:621–8.
- 3 Griffiths M, Sanderson D, Penna LK. Cervical epithelial abnormalities among women with vulval warts—no more common than among controls. *Int J Gynaecol Cancer* (In Press).

Rowen *et al* have looked at an important issue regarding the relationship between genital warts and cervical cancer.

There are a number of small points in respect of the data they present which require clarification: the indications for taking a cervical smear are actually not given and it is not clear whether the 185 patients represent the total number smeared over the 5 month period of study. It is really quite important to know who was invited to participate and who declined.

The proportion of abnormal smears was much lower in the non-wart group (7 of 55) than in the wart group (52 of 117). However, the wart group is twice the size of the non-wart group, which may not be representative of women patients as a whole.

Although it is clearly stated that 59 patients had a cervical biopsy, it is less clear how many were colposcoped. Surely some patients with abnormal smears showed no abnormality on colposcopy and therefore did not have a biopsy. If these patients are included in table 3, it is not clear from the legend, but 65 (117–52) patients seem to have gone missing.

While the authors’ conclusions appear valid from the data they present, the relevance of mildly abnormal smears is called into question. Their biopsy results show that cervical intra-epithelial neoplasia (CIN) was present in 30% (13 of 43) of patients with warts, 11% (1 of 9) of patients in contact with warts, but in 43% (3 of 7) of patients without warts or wart contact. From this it could well be concluded that genital warts are not related to CIN.

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Rowen *et al* reply:

The letters from Drs Griffiths, Evans and Kell concerning our recent paper are read with interest and raise some points which merit discussion. In our study the screeners were aware of clinical details. It is of course possible to over report smears. However, we do not feel that significant numbers are over reported as several safeguards are in place to prevent this. Firstly, a relatively junior screener cannot send out an abnormal report without the smear being reviewed by a senior screener. Secondly, a smear deemed to show mild dyskaryosis must be reviewed by a pathologist. Thirdly, follow-up smears from women with borderline abnormalities on previous smears are screened by a senior MLSO. If any abnormality is found on that smear, it and the previous smear are then reviewed by the cytopathologist. Furthermore, if there were significant over reporting one might suspect that the “current smear normal, previous smear abnormal” group in our study would be larger than we found.

Dr Griffiths’ results from his pilot study in which screeners were blinded to the real clinical details are of interest. There may or may not be an excess of smears reported as abnormal in the “warts” group. However his conclusion that the failure to demonstrate a statistically significant difference in rates of smears reported as abnormal in the two groups was simply due to sample size cannot be justified at this stage. If a full scale study, with sufficient numbers in each group subsequently demonstrates a significant difference in rates, then one may draw the conclusion that the pilot study failed to demonstrate significant differences because of sample sizes.

With regard to the points raised by Drs Evans and Kell. Patients attending our clinic are offered cervical cytology if (a) they have not had a smear within the last 3 years or (b) they or their sexual partners have genital warts and they have not had a smear within one year. The 185 women in the study were drawn from 191 women having smears during the study period. No patients declined to answer the life-style questions, but six patients, all from the warts/warts contact group were not offered colposcopy appointments as they were about to leave the area and thus were not included in the study.

All patients in the study with abnormal smears, except two, who defaulted from follow up, were colposcoped, as were all, except 3 from the warts/warts contact group who had normal smears.

Table 3 in the paper should have been headed “Abnormal cytology results compared with colposcopy results” and “Biopsy proven CIN”. Thus the NO CIN column represents those whose biopsies were negative and those who had a normal colposcopy and were therefore not biopsied. We apologise for the confusion this may have caused.

In the small number of women with abnormal smears but no history of warts or wart contact, we would agree that there was a high rate of CIN. They did however differ from other groups by virtue of having significantly more sexual partners and it is possible some may have been infected with HPV without developing warts. What is not known is the natural history of sub-clinical HPV infection and whether such lesions ultimately develop into frank warts or aceto-white lesions and if not, whether these sub-clinical lesions are also associated with abnormal cytology in the absence of warts.

We also agree that we did not find a significant incidence of CIN in the warts/warts contact groups, a point alluded to in the discussion. We did find differences in rates of cytological abnormalities between the warts/warts contact group and the non wart/wart contact group and forward the notion that these abnormalities may be the result of an acute reaction to HPV infection which had settled by the time colposcopy was performed.

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Increased evidence of cervical cytological abnormalities in women with genital warts

We read with great interest Dr Rowen *et al*’s¹ paper examining the need for increased cytological vigilance in women with genital warts or contact with genital warts, and agree that this group should also be offered colposcopic examination of the cervix irrespective of their cervical cytology result. Our results and experience are in agreement with the above conclusion. We present figures from our department on women with genital warts and negative cytology. In the period May 1987 to June 1988, 248 women with genital warts and 12 with wart contacts, attending the genitourinary medicine out-patient clinic, Royal Liverpool University Hospital